

**REMARKS**

**I. Outstanding Rejections**

Claims 1, 2, 4, 5, 8-18 and 20-24 stand rejected under 35 U.S.C. § 103(a) as being obvious over Frey II (U.S. Patent Application Publication No. 2003/0072793) in view of Beers (The Merck Manual of Diagnosis and Therapy, 17<sup>th</sup> Edition, pp 1525-1539 and pp 1932-1933, 1999).

Claims 1, 2, 4, 5, 11-15 and 20-24 stand rejected under 35 U.S.C. § 103(a) as being obvious over Siuciak (U.S. Patent No. 5,599,560) in view of Beers.

**II. Patentability Arguments**

A. The Rejection of Claims 1, 2, 4, 5, 8-18, and 20-24 under 35 U.S.C. § 103(a) over Frey II in view of Beers Should Be Withdrawn Because Frey II is Directed to a Mode of Drug Administration and Not to Methods of Disease Treatment

The rejection of claims 1, 2, 4, 5, 8-18 and 20-24 should be withdrawn because Frey II discloses a laundry list of “agents” for the treatment of a laundry list of “disorders,” but fails to teach or suggest that any one of the recited agents can be used in the treatment of a specific disorder much less those disorders recited in independent claims 1 or 15. This is hardly surprising because Frey II is directed to a mode of drug administration and not to methods of disease treatment.

Frey II is directed to a particular method of transporting or delivering an agent to the central nervous system (CNS) of a subject. That method calls for administration of an agent by way of a tissue innervated by the trigeminal nerve that is outside of the nasal cavity. The examples only relate to administration of Insulin-like Growth Factor-I. Accordingly, the list of agents (see Frey II, paragraphs 0036-0104) that could be administered by the recited method and the list of conditions (See, Frey II, paragraph 0169) for which it might be desirable to directly administer drugs to the CNS is not prescriptive.<sup>1</sup> Indeed, most of the forty plus agents listed would not be expected to be therapeutic for most of the seventeen or more conditions listed in paragraph 0169. Some combinations of agent and condition may also be contraindicated. Accordingly, one of skill in the art would not have concluded which one of the many “agents” disclosed in Frey II could be used to alleviate one or more symptoms of a psychological disorder.

Beers, a textbook for the diagnosis and therapy of various disorders, teaches that depression is in the same class as affective disorders and that premenstrual syndrome (PMS) is characterized by *inter alia* anxiety and depression. Beers does not teach or suggest the use of NGF for the treatment of depression, anxiety disorders, panic attacks, premenstrual dysphoric disorder (PMDD), and premenstrual syndrome (PMS), sleep disorders, tension headaches, and constipation or the symptoms associated with those disorders. Consequently, Beers fails to make up for the

<sup>1</sup> There are at least 680 different therapeutic agent/CNS disorder combinations implied by the Examiner’s argument.

deficiencies of Frey II (i.e., method of alleviating one or more symptoms of a psychological disorder by administering NGF).

Not only does Frey II provide no disclosure for the use of NGF to alleviate the symptoms associated with the specific psychological disorders of independent claim 1, it especially makes no mention of alleviating the symptoms of sleep disorders, tension headaches, and constipation as recited in independent claim 15.

The only motivation or suggestion to use NGF to alleviate the symptoms of a psychological disorder arises out of the instant application and it is impermissible to use the applicants' own disclosure to find a motivation for the claimed invention, as this would be the epitome of hindsight reconstruction. See, M.P.E.P. § 2141. For these reasons, applicants respectfully submit that the articulated rejection fails to establish *prima facie* obviousness for the subject matter of any of claims 1, 2, 4, 5, 8-18 and 20-24 under 35 U.S.C. § 103(a) over Frey II in view of Beers. Accordingly, the rejection may properly be withdrawn.

B. The Rejection of Claims 1, 2, 4, 5, 11-15 and 20-24 under 35 U.S.C. § 103(a) over Siuciak in view of Beers Should Be Withdrawn Because Siuciak Does Not Teach the Use of NGF for Treatment of Psychological Disorders

Siuciak does not teach the use of NGF and the Examiner's reliance on Siuciak for allegedly teaching the use of all members of the nerve growth factor family for the treatment of psychological disorders is improper because Siuciak itself emphasizes the different biological activities of NGF when compared to neurotrophin-3 (NT-3), neurotrophin-4 (NT-4) and brain-derived neurotrophic factor (BDNF) used therein. Thus, Siuciak itself contradicts the Examiner's apparent assertion that all members of the neurotrophin family can be used interchangeably.

In fact, at column 3, lines 11-14, Siuciak refers to a study by Friedmann et al. (Exp. Neph., 119:72-78, 1999, set forth in Exhibit A) which reports that

Specific neurotrophins such as **NT-3 and NT-4 enhanced survival of both neuronal populations** [locus coeruleus (LC) and basal forebrain (BF)]. **NGF, which has no effect on LC neurons**, influenced the BF by increasing cholinergic function but not survival, **in contrast to BDNF, NT-3, and NT-4.** (page 76, second column, first full paragraph, emphasis added.)

Thus, Friedmann discloses that members of the NGF family of neurotrophins can exhibit different biological activities. Accordingly, one of skill in the art would not have concluded from Siuciak, which only discloses the use of BDNF, NT-3 and NT-4 for the treatment of depression, that NGF could be expected to have the same biological activity as BDNF, NT-3 and NT-4. Similarly, one of skill on the art would not have concluded from Siuciak that NGF could be used as a therapeutic in disorders normally treated with BDNF, NT-3 or NT-4 and would not be motivated upon

review of Siuciak to use NGF to alleviate the symptoms of the psychological disorders recited in independent claims 1 or 15.

Beers is merely a textbook for the diagnosis and therapy of various disorders and teaches that depression is in the same class as affective disorders and that premenstrual syndrome (PMS) is characterized by *inter alia* anxiety and depression. As such Beers fails to make up for the deficiencies of Siuciak because it does not teach or suggest the use of NGF for the treatment of depression, anxiety disorders, panic attacks, premenstrual dysphoric disorder (PMDD), and premenstrual syndrome (PMS) or the symptoms associated with those disorders.

Not only does Siuciak provide no disclosure for the use of NGF to alleviate the symptoms associated with the specific psychological disorders of independent claim 1, it especially makes no mention of alleviating the symptoms of sleep disorders, tension headaches, and constipation as recited in independent claim 15.

The only motivation or suggestion to use NGF to alleviate the symptoms of a psychological disorder arises out of the present application and it is impermissible to use the applicants' own disclosure to find a motivation for the claimed invention, as this would be the epitome of hindsight reconstruction. See MPEP § 2141. For these reasons, applicants respectfully submit that the articulated rejection fails to establish *prima facie* obviousness.

Finally, it should be noted that in response to the previous Office Action, applicants did not "argue that NGF illustrates typical qualities of neurotrophic factors and neurotrophin family" as asserted by the Examiner. In contrast, applicants stated that NGF is a different protein than BDNF, NT-3 and NT-4. Accordingly, in the absence of evidence that NGF successfully treats psychological conditions and in the presence of evidence that NGF has different activities from NT-3, NT-4 and BDNF, the rejection based on Siuciak should be withdrawn.

For the foregoing reasons, Applicants submit that the Examiner has failed to establish a *prima facie* case of obviousness for the subject matter of any of claims 1, 2, 4, 5, 11-15 and 20-24 under 35 U.S.C. § 103(a) over Siuciak in view of Beers. Accordingly, the rejection may properly be withdrawn.

### **III. Conclusion**

For the foregoing reasons, Applicants request withdrawal of all outstanding rejections and allowance of the pending claims. No other fees are believed to be due with the filing of this paper. However, the Director is authorized to charge any additional fees deemed necessary to Deposit Account No. 13-2855, under order number 13024/38627A.

If the examiner believes that a telephone conversation would expedite allowance of the claims, he is invited to contact the undersigned agent or Jeffrey S, Sharp, attorney for applicants, at the number below.

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Respectfully submitted,

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